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4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 876

[Docket No. FDA-2012-N-0303]

Gastroenterology-Urology Devices; Reclassification of Implanted Blood Access Devices

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to reclassify the implanted blood access device preamendments class III device into class II (special controls). FDA is proposing this reclassification on its own initiative based on new information. FDA is taking this action under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments), the Safe Medical Devices Act of 1990 (SMDA), the Food and Drug Administration Modernization Act of 1997 (FDAMA), and the Medical Device User Fee and Modernization Act of 2002 (MDUFMA).

DATES: Submit either electronic or written comments on the proposed rule by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Please see section XIII of this document for the effective date of any final rule that may publish based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. FDA-2012-N-0303 by any of the following methods, except that comments on information collection issues under the Paperwork

Reduction Act of 1995 must be submitted to the Office of Regulatory Affairs, Office of Management and Budget (OMB) (see the “Paperwork Reduction Act of 1995” section of this document).

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301-827-6870.
- Mail/Hand delivery/Courier (for paper, disk, or CD-ROM submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Agency name and docket number for this rulemaking. All comments received may be posted without change to <http://www.regulations.gov>, including any personal information provided. For additional information on submitting comments, see the “Comments” heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background--Regulatory Authorities

The FD&C Act, as amended by the 1976 amendments (Public Law 94-295), the SMDA (Public Law 101-629), the FDAMA (Public Law 105-115), the MDUFMA (Public Law 107-250), the Medical Devices Technical Corrections Act (Public Law 108-214), and the Food and Drug Administration Amendments Act of 2007 (Public Law 110-85), establish a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the FD&C Act, devices that were in commercial distribution before the enactment of the 1976 amendments, May 28, 1976 (generally referred to as preamendments devices), are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as postamendments devices) are automatically classified by section 513(f) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless, and until, the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

A preamendments device that has been classified into class III may be marketed by means of premarket notification procedures (510(k) process) without submission of a premarket approval application (PMA) until FDA issues a final regulation under section 515(b) of the FD&C Act (21 U.S.C. 360e(b)) requiring premarket approval.

Section 513(e) of the FD&C Act governs reclassification of classified preamendments devices. This section provides that FDA may, by rulemaking, reclassify a device (in a proceeding that parallels the initial classification proceeding) based upon “new information.” FDA can initiate a reclassification under section 513(e) of the FD&C Act or an interested person may petition FDA to reclassify a preamendments device. The term “new information,” as used in section 513(e) of the FD&C Act, includes information developed as a result of a reevaluation of the data before the Agency when the device was originally classified, as well as information not presented, not available, or not developed at that time. (See, e.g., Holland Rantos v. United States Department of Health, Education, and Welfare, 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); Upjohn v. Finch, 422 F.2d 944 (6th Cir. 1970); Bell v. Goddard, 366 F.2d 177 (7th Cir. 1966).)

Reevaluation of the data previously before the Agency is an appropriate basis for subsequent regulatory action where the reevaluation is made in light of newly available regulatory authority (see Bell v. Goddard, supra, 366 F.2d at 181; Ethicon, Inc. v. FDA, 762 F.Supp. 382, 389-391 (D.D.C. 1991)) or in light of changes in “medical science.” (See Upjohn v. Finch, supra, 422 F.2d at 951). Whether data before the Agency are past or new data, the “new information” to support reclassification under section 513(e) must be “valid scientific evidence,” as defined in section 513(a)(3) of the FD&C Act and 21 CFR 860.7(c)(2). (See, e.g., General Medical Co. v. FDA, 770 F.2d 214 (D.C. Cir. 1985); Contact Lens Assoc. v. FDA, 766 F.2d 592 (D.C. Cir.), cert. denied, 474 U.S. 1062 (1985)).

FDA relies upon “valid scientific evidence” in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the valid scientific evidence upon which the Agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA. (See section 520(c) of the FD&C Act (21 U.S.C. 360j(c).) Section 520(h)(4) of the FD&C Act, added by FDAMA, provides that FDA may use, for reclassification of a device, certain information in a PMA 6 years after the application has been approved. This includes information from clinical and preclinical tests or studies that demonstrate the safety or effectiveness of the device but does not include descriptions of methods of manufacture or product composition and other trade secrets.

FDAMA added a new section 510(m) to the FD&C Act. New section 510(m) of the FD&C Act provides that a class II device may be exempted from the premarket notification requirements under section 510(k) of the FD&C Act, if the Agency determines that premarket notification is not necessary to assure the safety and effectiveness of the device.

II. Regulatory History of the Device

In the preamble to the proposed rule (46 FR 7616, January 23, 1981), the Gastroenterology-Urology Devices Panel recommended that both implanted and nonimplanted blood access devices be classified into class II. Although FDA agreed with the panel recommendation for nonimplanted blood access devices, FDA disagreed with the panel for implanted blood access devices and proposed that implanted blood access devices be classified into class III because FDA believed that the device presented a potential unreasonable risk of illness or injury to the patient if there are not adequate data to assure the safe and effective use of the device. FDA also noted that the implanted blood access device is part of a life-supporting and life-sustaining system and that general controls and performance standards were insufficient to provide reasonable assurance of the safety and effectiveness of implanted blood access devices. In 1983, FDA classified implanted blood access devices into class III, but the accessories to these devices into class II (48 FR 53012, November 23, 1983). In 1987, FDA published a clarification by inserting language in the codified language stating that no effective date had been established for the requirement for premarket approval for implanted blood access devices (52 FR 17732 at 17738, May 11, 1987).

In 2009, FDA published an order for the submission of information on implanted blood access devices (74 FR 16214, April 9, 2009). In response to that order, FDA received information in support of reclassification from 15 device manufacturers who all recommended that implanted blood access devices be reclassified to class II. The manufacturers stated that safety and effectiveness of these devices may be assured by bench testing, biocompatibility testing, sterility testing, expiration date testing, labeling, and standards.

III. Device Description

Implanted blood access devices include various flexible or rigid tubes, such as catheters, cannulae or hollow needles. Chronic hemodialysis catheters are soft, blunt-tipped plastic catheters that have a subcutaneous “cuff” for tissue ingrowth. They are placed in a central vein to allow blood access. Chronic hemodialysis catheters serve as conduits for the removal of blood from the patient, delivery to a hemodialysis machine for filtering, and return of filtered blood to the patient. They have no moving parts, consisting, essentially, of flexible tubing terminating in rigid Luer lock connectors for attachment to a dialysis machine. Subcutaneous catheters are totally implanted below the skin surface with no external communication. AV Shunts and Vessel Tips are tubing with tapered tips that are inserted into the artery and vein. The tubing is attached to the roughened or etched outer surface of the tip. The tubing is external to the skin and can be accessed with needles. They are similar to the subcutaneous catheters.

IV. Proposed Reclassification

FDA is proposing that the device subject to this proposal be reclassified from class III to class II. FDA believes that the identified special controls would provide reasonable assurance of safety and effectiveness. Therefore, in accordance with sections 513(e) and 515(i) of the FD&C Act and 21 CFR 860.130, based on new information with respect to the devices, FDA, on its own initiative, is proposing to reclassify this preamendments class III device into class II. The Agency has identified special controls that would provide reasonable assurance of their safety and effectiveness. FDA has considered implanted blood access devices in accordance with the reserved criteria and decided that the device does require premarket notification. The Agency does not intend to exempt this proposed class II device from premarket notification (510(k)) submission as provided for under section 510(m) of the FD&C Act.

V. Risks to Health

After considering the information from the reports and recommendations of the advisory committees (panels) for the classification of these devices along with information submitted in response to the 515(i) order and any additional information that FDA has encountered, FDA has evaluated the risks to health associated with the use of implanted blood access devices and determined that the following risks to health are associated with its use:

1. Thrombosis in patient and catheter. Inadequate blood compatibility of the materials used in this device, blood pooling between dialysis sessions, or turbulent blood pathways could lead to potentially debilitating or fatal thromboembolism.
2. Adverse tissue reaction. Inadequate tissue compatibility of the materials used in this device could cause an immune reaction.
3. Infection and pyrogen reactions. An improperly sterilized device could cause an infection or an unclean device could cause a fever.
4. Device failure. Weakness of connections or materials could lead to blood loss.
5. Cardiac Arrhythmia, hemorrhage, embolism, nerve injury, or vessel perforation. Improper placement into the heart or blood vessel could damage tissues and result in injuries.
6. Hemolysis. The destruction of red blood cells due to turbulence or high pressure created by narrow openings or changes in blood flow paths.

VI. Summary of Reasons for Reclassification

FDA believes that implanted blood access devices should be reclassified into class II because special controls, in addition to general controls, can be established to provide reasonable

assurance of the safety and effectiveness of the device. In addition, there is now adequate effectiveness information sufficient to establish special controls to provide such assurance.

VII. Summary of Data Upon Which the Reclassification is Based

Since 1987 when FDA classified implanted blood access devices into class III, sufficient evidence has been developed to support a reclassification to class II with special controls. FDA has been reviewing these devices for many years and their risks are well known. The risks include clotting, infection, and breakage of the materials, and these risks can be adequately mitigated by special controls. Catheters continue to evolve over time with improved materials and insertion techniques. A review of 15 publications shows a decrease in infections and an increase in patency over three decades (1980 to 2010) (Refs. 2-16). FDA believes that special controls currently in use can ensure the safety and effectiveness of implanted blood access devices.

VIII. Proposed Special Controls-Related Documents

FDA believes that the special controls as described in the guidance document “Class II Special Controls Guidance Document: Implanted Blood Access Devices for Hemodialysis” (Ref. (1)) are sufficient to mitigate the risks to health described in section V of this document. Elsewhere in this issue of the Federal Register, FDA is announcing the availability of a draft guidance document that, when finalized, would serve as a special control, if FDA reclassifies this device. If adopted, following the effective date of a final rule classifying the device, any firm submitting a 510(k) pre-market notification for the device would need to address the issues covered in the special control guidance. However, the firm would need to show only that its device meets the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

IX. Environmental Impact

The Agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

X. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612) and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Orders 12866 and 13563 direct Agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The Agency believes that this proposed rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because reclassification of implanted blood access devices from class III to class II with special controls makes these devices' formal classification consistent with current FDA and industry practice, the Agency proposes to certify that the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is \$136 million, using the most current (2010) Implicit Price Deflator for the Gross Domestic

Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

FDA is proposing to reclassify implanted blood access devices from class III to class II with special controls. Typically, a class III device must be granted premarket approval by FDA. However, at the present time, implanted blood access devices are handled in a fashion similar to class II devices, with manufacturers receiving clearance to market via a 510(k) and no PMA requirement. Hence, this rule brings the formal classification of implanted blood access devices into line with current practice and will likely cause little to no change in behavior on the part of industry, consumers, or FDA. There remains the possibility that some new actions will be required of industry in light of the formalization of class II special controls. To the extent that manufacturers are not already complying with the recommendations contained in the special controls guidance document, manufacturers will incur additional costs, which may then be passed on to consumers or insurance payers in the form of higher prices. We anticipate that such costs will be negligible, however, because the proposed special controls for labeling, safety, and performance testing reflect current FDA requirements for marketing clearance of implanted blood access devices.

FDA has already recognized that the 510(k) premarket notification process is sufficient for ensuring the safety and effectiveness of these products. Firms have not been required to submit PMAs or meet other requirements typically expected of manufacturers of class III devices, and the Agency expects that continuing the current 510(k) clearance process will pose no new risks to consumers. FDA requests comment on this issue and on all costs and benefits of the proposed reclassification.

XI. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive

Order 13132. Section 4(a) of the Executive order requires Agencies to "construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute." Federal law includes an express preemption provision that preempts certain state requirements "different from or in addition to" certain Federal requirements applicable to devices. (See section 521 of the FD&C Act (21 U.S.C. 360k); Medtronic, Inc. v. Lohr, 518 U.S. 470 (1996); and Riegel v. Medtronic, Inc. 128 S. Ct. 999 (2008)). If this proposed rule is made final, the special controls established by the final rule would create "requirements" for specific medical devices under 21 U.S.C. 360(k), even though product sponsors have some flexibility in how they meet those requirements (Cf. Papike v. Tambrands, Inc., 107 F.3d 737, 740-742 (9th Cir. 1997)).

XII. Paperwork Reduction Act of 1995

This proposed rule refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 812 have been approved under OMB control number 0910-0078; the collections of information in part 807 subpart E have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 814 subpart B have been approved under OMB control number 0910-0231; and the collections of information under 21 CFR part 801 have been approved under OMB control number 0910-0485.

XIII. Proposed Effective Date

FDA is proposing that any final rule based on this proposal become effective on the date of its publication in the Federal Register or at a later date if stated in the final rule.

XIV. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

XV. References

The following reference has been placed on display in the Division of Dockets Management (see ADDRESSES), and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site address, but we are not responsible for any subsequent changes to the Web site after this document publishes in the Federal Register.)

1. Draft guidance entitled “Class II Special Controls Guidance Document: Implanted Blood Access Devices for Hemodialysis,” available at

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>

2. Eisenhower ED, Derveloy RJ, Hastings PR: Prospective evaluation of central venous pressure (CVP) catheters in a large city-county hospital. *Ann Surg* 196:560-564, 1982.
3. Vanholder V, Hoenich N, Ringoir S: Morbidity and mortality of central venous catheter hemodialysis: a review of 10 years' experience. *Nephron* 47:274-279, 1987.
4. Almirall J, Gonzalez J, Rello J, Campistol JM, Montoliu J, Puig de la Bellacasa J, Revert L, Gatell JM: Infection of hemodialysis catheters: incidence and mechanisms. *Am J Nephrol* 9:454-459, 1989.
5. Boyle MJ, Gawley WF, Hickey DP, Drumm J, Murphy DM, Hanson JS, Glacken P: Experience using the Quinton Permcath for haemodialysis in the Irish Republic. *Nephrol Dial Transplant* 12:1934-1939, 1997.
6. Randolph AG, Cook DJ, Gonzales CA, Pribble CG: Ultrasound guidance for placement of central venous catheters: a meta-analysis of the literature. *Crit Care Med* 24:2053-2058, 1996.
7. Arnold WP: Improvement in hemodialysis vascular access outcomes in a dedicated access center. *Semin Dial*

13:359-363, 2000.

8. Wivell W, Bettmann MA, Baxter B, Langdon DR, Remilliard B, Chobanian M: Outcomes and performance of the Tesio twin catheter system placed for hemodialysis access. *Radiology* 221:697-703, 2001.
9. Lund GB, Trerotola SO, Scheel PF Jr, Savader SJ, Mitchell SE, Venbrux AC, Osterman FA Jr: Outcome of tunneled hemodialysis catheters placed by radiologists. *Radiology* 198:467-472, 1996.
10. Trerotola SO, Johnson MS, Harris VJ, Shah H, Ambrosius WT, McKusky MA, Kraus MA: Outcome of tunneled hemodialysis catheters placed via the right internal jugular vein by interventional radiologists. *Radiology* 203:489-495, 1997.
11. Prabhu PN, Kerns SR, Sabatelli FW, Hawkins IF, Ross EA: Long-term performance and complications of the Tesio twin catheter system for hemodialysis access. *Am J Kidney Dis* 30:213-218, 1997.
12. Schnabel KJ, Simons ME, Zevallos GF, Pron GE, Fenton SS, Sniderman KW, Vanderburgh LC: Image-guided insertion of the Uldall tunneled hemodialysis catheter: technical success and clinical follow-up. *J Vasc Interv Radiol* 8:579-586, 1997.
13. Nassar GM, Ayus JC: Infectious complications of the hemodialysis access. *Kidney Int* 60:1-13, 2001 (1990s data).
14. Power A, Singh SK, Ashby D, Cairns T, Taube D, Duncan N: Long-term Tesio catheter access for hemodialysis can deliver high dialysis adequacy with low complication rates. *J Vasc Interv Radiol* 22:631-637, 2011.
15. Duncan ND, Singh S, Cairns TD, Clark M, El-Tayar A, Griffith M, Hakim N, Hamady M, McLean AG, Papalouis V, Palmer A, Taube D: Tesio-Caths provide effective and safe long-term vascular access. *Nephrol Dial Transplant* 19:2816-2822, 2004.
16. Eisenstein I, Tarabeih M, Magen D, Pollack S, Kassis I, Ofer A, Engel A, Zelikovic I: Low infection rates and prolonged survival times of hemodialysis catheters in infants and children. *Clin J Am Soc Nephrol* 6:793-798, 2011.

List of Subjects in 21 CFR Part 876

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 876 be amended as follows:

PART 876—GASTROENTEROLOGY-UROLOGY DEVICES

1. The authority citation for 21 CFR part 876 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

2. Section 876.5540 is amended by revising paragraphs (a)(1), (a)(2), and (b)(1) and by removing paragraph (c) to read as follows:

§ 876.5540 Blood access device and accessories.

(a) * * *

(1) The implanted blood access device consists of various flexible or rigid tubes, such as catheters, or cannulae, which are surgically implanted in appropriate blood vessels, may come through the skin, and are intended to remain in the body for 30 days or more. This generic type of device includes: Single, double, and triple lumen catheters with cuffs, subcutaneous ports with catheters, shunts, cannula, vessel tips, and connectors specifically designed to provide access to blood.

(2) The nonimplanted blood access device consists of various flexible or rigid tubes, such as catheters, cannulae or hollow needles, which are inserted into appropriate blood vessels or a vascular graft prosthesis (§§ 870.3450 and 870.3460), and are intended to remain in the body for less than 30 days. This generic type of device includes noncuffed catheters, fistula needles, single dialysis needles (coaxial flow needle), and the single needle dialysis set (alternating flow needle).

* * * * *

(b) Classification. (1) Class II (special controls) for the implanted blood access device. The special control for this device is FDA's "Class II Special Controls Guidance Document: Implanted Blood Access Devices for Hemodialysis."

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Dated: June 15, 2012.

Nancy K. Stade,

Deputy Director for Policy,
Center for Devices and Radiological Health.

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